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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,323	03/05/2002	Manfred Schmitt	100564-00082	5188

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EXAMINER	
HELMS, LARRY RONALD	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,323	SCHMITT ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-39* is/are pending in the application.

4a) Of the above claim(s) *36-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☑ Other: NOTICE TO COMPLY

DETAILED ACTION

1. The request filed on 4/14/05 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/926323 is acceptable and a RCE has been established. Claims 30-39 are pending and claims 30-35 are currently under prosecution. An action on the RCE follows.

2. Claims 30, 34-35 have been amended.

3. Claims 36-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Election was made **without** traverse in Paper filed 5/10/04.

4. Claims 30-35 are under examination.

5. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

6. The following Office Action contains NEW GROUNDS of Rejections.

Sequence Compliance

7. The amendment filed 3/16/05 added claims that recited SEQ ID NOs 7-10. The sequence listing does not contain separate SEQ ID NOs for these sequences. However, a proper search could be performed because SEQ ID NO:7 corresponds to residues 31-35 of SEQ ID NO:2, SEQ ID NO:8 corresponds to residues 24-30 of SEQ ID NO:4, SEQ ID NO:9 corresponds to residues 50-65 of SEQ ID NO:2, and SEQ ID NO:10 corresponds to residues 50-56 of SEQ ID NO:4. Although a proper search could

be performed this application is not in sequence compliance because it does not contain the recited SEQ ID NOs. As such a sequence compliance form is included in this Office Action.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth above. Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply.

APPLICANT IS GIVEN THE TIME ALLOTED IN THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Rejections Withdrawn

8. The rejection of claims 34-35 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description is withdrawn in view of the amendments to the claims and the showing of all 6 CDRs of the IIIF10 antibody.

9. The rejection of claims 34-35 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of arguments.

10. The rejection of claim 35 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment to the claim.

11. The rejection of claims 34-35 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

Response to Arguments

12. The rejection of claims 30-35 under 35 U.S.C. 103(a) as being unpatentable over Dano et al (US Patent 5,519,120, issued 5/96) and further in view of Luther et al (American Journal of Pathology 150:1231-1244, 1997, IDS 10/15/01) and Heiss et al

(Nature Medicine 1:1035-1039, 1995, IDS 10/15/01) and Terstappen (US Patent 5,234,816, issued 8/93, IDS 10/15/01) is maintained.

The response filed 3/16/05 has been carefully considered but is deemed not to be persuasive. The response states that although Luther's antibody may inherently bind to the recited epitope, there is no suggestion in Luther that his antibody binds to the epitope 52-60 of human uPAR and can be used to diagnose tumors and one skill in the art would not reasonably have expected Luther's antibody to be useful for differentiating between tumor and normal cells based on the disclosures of Dano, Heiss, Luther, and Terstappen (see page 6 of response). In response to this argument, the antibody of Luther is in fact the same antibody as in the instant application and does bind residues 52-60 in human uPAR (see abstract). Thus, it is not only inherent that the antibody of Luther binds to the recited epitope, it is explicitly taught. Although Luther does not explicitly state that the IIIF10 antibody discriminates between uPAR on tumor and normal cells, this would be an inherent feature of the IIIF10 antibody since it binds to this epitope as recited in the claims. The claims require an antibody that binds the epitope of residues 52-60 of human uPAR to diagnose tumor and the active steps are contacting the sample with an antibody that binds to the recited epitope and binding is indicative of a tumor. Luther teaches the same antibody claimed in claims 34-35 which would have the same recited CDRs and binds to the recited epitope. Therefore, the antibody of Luther would inherently discriminate between uPAR on normal and tumor as required in the claims. The response further states that Dano's antibody does not differentiate between tumor and normal uPAR (see page 6 of response). In response to

this argument, the antibody of Luther has this property as stated above. In addition, because of the indefinite nature of the amended claims (see 112 second below) the binding of the antibody of Luther's would be indicative of a tumor and give an indication of the prognosis of the cancer (higher signal in the assay would indicate more antibody binding to the tumor cells and increased course of the tumor infiltration).

The following is a NEW GROUND of Rejection

13. Claims 30-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 30 is indefinite for reciting "gives a prognosis for the cause of a malignant disease". It is unclear how binding of the antibody can give a "cause" for a cancer. Does the phase mean that the binding can give the "cause" such as smoking or contacts with chemicals or mutagens or some other "cause"?

14. Claims 30-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

This is a new matter rejection.

Claim 30 has been amended to recite "discriminates between uPAR on normal and tumor cells" and "gives a prognosis for the cause of a malignant disease". The response filed 3/16/05 did not indicate where support for such phrases could be found in the specification as originally filed. The specification discloses on page 6 that the IIIF10 antibody has an affinity for a tumor cell-specific uPAR "which is at least comparable to that for a uPAR from normal cells". This similar statement is on page 8-9 bridging paragraph again stating "comparable affinity". Thus, the specification indicates that the antibody is of comparable affinity and not discriminates between uPAR on normal and tumor.

Claim 30 has been amended to recite "gives a prognosis for the cause of a malignant disease". There is not support for such a phase and on page 21 the specification discloses "measured with the IIIF10/HU277-ELISA have a significant prognostic relevance for the course of the disease". Thus it appears that there is no support for the "cause" of the disease. Applicants are required to provide specific support for the claimed limitations or remove them from the claims.

15. Claims 30-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing tumors with an antibody that binds to residues 52-60 in human uPAR and binding of the antibody to human uPAR is indicative of diagnosis, does not reasonably provide enablement for a method of diagnosing tumors with binding of an antibody to residues 52-60 in human uPAR and binding gives a cause of the tumor. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a method of diagnosing tumor by an antibody binding method and the binding indicates a cause for the tumor.

The specification discloses an ELISA using the IIIF10 antibody to human uPAR using tumor samples and there is no indication of the cause of the tumor (see pages 19-20). The specification does not disclose a method for the cause of a tumor.

The claims are not commensurate with the enablement provided in the specification. It is well established in the art that determining the cause of a tumor is nearly impossible. Tumors are thought to originate from possibly many causes such as smoking, environmental exposure to chemicals, and genetics, for example. The art does not recognize a specific cause or methods to determine a specific cause from an ELISA assay alone as indicated in the specification. There is no indication in the specification or in the prior at that an ELISA for uPAR would be able to give a cause for the tumor.

Therefore, in view of the lack of predictability in the art and in the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the broadly claimed invention.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached on (571) 272-0787.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832

LARRY R. HELMS, PH.D
PRIMARY EXAMINER

Application No. 09/926323

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE